

WHAT IS CLAIMED IS:

1. A method for inhibiting tumor growth in a mammalian host expressing native NKG2D and determined to harbor a tumor arising in situ and comprising tumor cells, the method comprising steps:

5            administering to the mammalian host a composition comprising a multivalent NKG2D-binding agent, wherein the administering step is effective to inhibit growth of the tumor; and detecting a resultant inhibition of growth of the tumor.

10          2. A method according to claim 1, wherein the tumor cells express a detectable amount of a native NKG2D ligand.

15          3. A method according to claim 1, wherein the tumor cells express a substantially undetectable amount of native NKG2D ligand.

4. A method according to claim 1, wherein the tumor cells are melanoma cells.

5. A method according to claim 1, wherein the tumor cells present downregulated MHC class I proteins.

20          6. A method according to claim 1, wherein the tumor cells are substantially non-immunogenic

7. A method according to claim 1, wherein the tumor cells are highly metastatic.

8. A method according to claim 1, wherein the tumor cells are highly tumorigenic.

25          9. A method according to claim 1, wherein the administering is remote from the tumor.

10. The method of claim 1, wherein the agent comprises a NKG2D-specific antibody.

30          11. The method of claim 1, wherein the agent comprises a NKG2D ligand comprising a plurality of covalently linked natural NKG2D binding moieties.

12. The method of claim 1, wherein the agent comprises a NKG2D ligand comprising a plurality of non-covalently linked natural NKG2D binding moieties, wherein the moieties are restricted to a common presenting surface.

5 13. The method of claim 1, wherein the agent comprises a NKG2D ligand comprising a plurality of non-covalently linked natural NKG2D binding moieties, wherein the moieties are restricted to a common presenting surface, wherein the common presenting surface is of a host-compatible cell transformed to express the binding moieties.

10 14. The method of claim 1, wherein the agent comprises a NKG2D ligand comprising a plurality of non-covalently linked natural NKG2D binding moieties, wherein the moieties are restricted to a common presenting surface, wherein the common presenting surface is of a host-compatible cell transformed to express the binding moieties, wherein one or more of the binding moieties are selected from the group consisting of MICA, MICB and ULBP ligand moieties.

15 15. The method of claim 1, wherein the agent comprises a multivalent NKG2D ligand comprising a plurality of non-covalently linked natural NKG2D ligand moieties, wherein the moieties are restricted to a common presenting surface, wherein the common presenting surface is of a host-compatible cell transformed to express the biding moieties, wherein the cell is derived from the tumor.

20 16. The method of claim 1, wherein the agent comprises a multivalent NKG2D ligand comprising a plurality of natural NKG2D ligand moieties, wherein one or more of the moieties are selected from the group consisting of MICA, MICB and ULBP ligand moieties.

25 17. The method of claim 1, wherein the agent comprises a NKG2D ligand comprising a plurality of non-covalently linked natural NKG2D binding moieties, wherein the moieties are restricted to a common presenting surface, wherein the common presenting surface is of a host-compatible cell transformed to express the binding moieties, wherein one or more of the binding moieties are selected from the group consisting of MICA, MICB and ULBP ligand moieties, wherein the cell is derived from the tumor.

18. A method for inhibiting tumor growth in a mammalian host expressing native NKG2D and determined to be predisposed to harboring a tumor arising in situ and comprising tumor cells, the method comprising steps:

administering to the mammalian host a composition comprising a multivalent NKG2D-

5 binding agent wherein the administration is effective to inhibit growth of the tumor; and

detecting a resultant inhibition of growth of the tumor.